REMARKS

Claims 1-3, 8-10, 18-20, and 38-49 are pending.

Applicants thank the Examiner for withdrawal of: the prior objections; prior rejection of claims 1-3, 8-10, 18-20, 38-44, and 46-48, under 35 U.S.C. 112 second paragraph; prior rejection of claims 1, 18, and 19, under 35 USC §102(a), as allegedly being anticipated by Doherty; prior rejection of claims 1, 18, 19, and 20, under 35 USC §102(e), as allegedly being anticipated by Doherty; and the prior rejection of claims 1 and 18-20 on the ground of nonstatutory obviousness-type double patenting.

Applicants thank the Examiner for indicating that claims 45-49 are allowed.

Applicants thank the Examiner for indicating that claims 3, 8-1-, 38-41, and 44 are objected to.

Claims 1, 2, 18-20, 42, and 43 stand rejected.

The Examiner maintained the rejection of claims 1, 2, 18-20, 42, and 43, under 35 U.S.C. 112 first paragraph, as allegedly comprising new matter in view of the recitation of SEQ ID NOS having respective particular polymorphic amino acid positions. Applicant respectfully traverses this rejection and has provided appropriate rebuttal argument.

No new matter has been added.

Claim Objections

The Examiner objected to claims 1, 8-10, 18, 38, and 39 in view of particular typographical errors.

Applicants have responsively amended claims 1, 8, 18, 38, and 39 to recite "Ala" in place of in inadvertently recited "Alu."

Applicants have responsively amended claims 8, 18, and 39 to recite "413" in place of in inadvertently recited "73."

The Examiner additionally objected to claims 1, 2, 18-20, 42, and 43 as depending from rejected claims. Applicants traverse this rejection, based on the below-described arguments relating to the Examiner's 35 U.S.C. 112 first paragraph-based rejection.

Applicants, therefore, respectfully request withdrawal of this rejection.

Rejections under 35 USC §112

The Examiner maintained the rejection of claims 1, 2, 18-20, 42, and 43, under 35 U.S.C. 112 first paragraph, as allegedly comprising new matter in view of the recitation of "wherein the polypeptide comprises: with respect to SEQ ID NO:14, at least one of the position 6 Pro and the position 73 Asp; with respect to SEQ ID NO:19, the position 2 Ser; with respect to SEQ ID NO:20, the position 5 Pro; with respect to SEQ ID NO:21, both the position 6 Leu and the position 73 Asp; with respect to SEQ ID NO:22, the position 16 Gln; with respect to SEQ ID NO:23, the position18 Leu; with respect to SEQ ID NO:24, the position 21 Asp, Ala or Val; with respect to SEQ ID NO:25, the position 36 Ile; with respect to SEQ ID NO:26, the position 54 Arg; with respect to SEQ ID NO:27, the position 64 Leu; or with respect to SEQ ID NO:28, both the position 6 Pro and the position 73 Asn."

The Examiner states that "it is noted that the rejection of the claims is not based on the finding that the specification fails to teach polypeptides that comprise the fragments as recited in the claims," and rather that "the current set of claims is an attempt to carve out a patentable portion of what is broadly disclosed in the specification." The Examiner states that "the specification discloses the sequences that are the polymorphisms of the previously disclosed Herstatin sequence," and further discloses "polypeptides that comprise any 50 to 79 contiguous amino acids from these

sequences, where the polypeptides bind to the ECD of HER-2 with an affinity binding constant of $10^8 M^{-1}$." The Examiner states, however, that "the specification fails to provide support for the limitation that the fragments must comprise the residues that are different from the previously disclosed Herstatin sequence" implying a "negative limitation," and that "by reciting limitations that require the claimed polypeptides that require a specific residue from a sequence, the claims are excluding fragments of 50 to 79 amino acids in length that are the same as fragments of 50 to 79 amino acids in length that have already been disclosed in the prior art (e.g., U.S. 6,414,130)." Based on this, the Examiner concludes "thus, the claims imply a negative limitation or an exclusionary proviso" and that MPEP 2173.05(i) states that any negative limitation or proviso must have a basis in the original disclosure," and that while applicants "while presenting evidence that the claimed polypeptides with respect to the polypeptides comprising the recited fragments are encompassed by the teachings of the specification, fail to provide support or a new genus of polypeptides that has been carved away from the originally disclosed genus."

Applicants respectfully traverse the Examiner's rejection based on the fact that the Applicants' above-described recitation is not a proviso clause, and even it is was, the Examiner, by her own acknowledgment, has misconstrued MPEP 2173.05(i) and U.S. patent law with respect to proviso clauses.

First, as an initial matter and as will be discussed in more detail below, contrary to the Examiner's urging, Applicants point out that there is nothing in U.S. patent law that prohibits an applicant to "carve out" a patentable portion of what is disclosed in the specification. Applicant is entitled to claim less than the full scope of the disclosure (see., e.g., In re Johnson, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) discussed below; and see also In re Wertheim, 191 USPQ 90, 97 (CCPA, 1976); and In re Saunders 170 USPQ 213, 220 (1971)), cited and discussed in the opinion of In re Johnson.

Second, Applicants point out that while the presently claimed genus (e.g., claim 1) may be *smaller* than that of original submitted claim 1, the claims as presently presented do not recite a negative limitation or proviso clause. Rather the claims are drawn to a genus of polypeptides that are fully supported, as discussed herein below, and for reasons already of record in Applicants' last Response and Amendment, that are reaffirmed and reasserted herein, and where the Examiner has moreover acknowledged based on this evidence that "the rejection is not based on the finding that the specification fails to teach polypeptides that comprise the fragments as recited in the claims."

Third, even were one to accept the Examiner's implication of a negative limitation or proviso clause into Applicants' presently claimed subject matter, contrary to the Examiner's urging, any such implied negative limitation or an exclusionary proviso has more than sufficient support in the original disclosure under 35 U.S.C. 112 first paragraph and MPEP 2173.05(i) (Negative Limitations) (cited by the Examiner), and according to U.S. case law specifically cited in MPEP 2173.05(i). Specifically, according to MPEP 2173.05(i), and as recognized by the Examiner:

> Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Note that a lack of literal basis in the specification for a negative limitation may not be sufficient to establish a *prima facie* case for lack of

> descriptive support. *Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993).

MPEP 2173.05(i). The Examiner's contention in the instant case is *contrary* to the holding and opinion In re Johnson, cited in MPEP 2173.05(i).

In re Johnson. In re Johnson (*attached hereto*) was an appeal from a decision of the Patent and Trademark Office Board of Appeals affirming, *inter alia*, a 35 U.S.C. 112 first paragraph written description rejection, based on alleged new matter in view of recitation of particular proviso clauses in claims drawn to a chemical genus of thermoplastic polyarylene polyether polymers (other rejections based on alleged indefiniteness and lack of enablement were also decided, but will not be discussed here). Specifically, with respect to alleged new matter, the substituent definitions of the genus claims at issue were amended to recite provisos that substituents E and E' may not both include a divalent sulfone group and may not both include a divalent carbonyl group linking two aromatic nuclei. The Board of Appeals had concluded that the "artificial subgenus" thus created in the claims was not described in the parent case[1] and would be new matter if introduced into the parent case, and would thus equally constitute "new matter," to the present application for which no antecedent basis existed in the parent case (*Id* at bottom of page 192).

The CCPA *reversed* this Board's of Appeals conclusion despite the fact that such proviso clauses were not present in the original applications at issue (see discussion under "***II***" on page 195). Specifically, the appellate court found "more than ample basis for claims of such scope" the opinion stating that the disclosure was clearly directed to polymers of the type claimed, that fifty specific choices (e.g., species) were mentioned for the E precursor compound, that a broad *class* was identified as embracing suitable *choices* for the E' precursor compound, that twenty-six "examples" were disclosed which detailed fifteen species of polyarylene polyethers, that only

[1] In re Johnson involved an interference proceeding wherein the question of granting priority to a parent case was at issue.

fourteen of those species and twenty-three of the "examples" were within the scope of the claims on appeal, and that two of the many choices for E and E' precursor compounds are deleted from the protection sought, "because appellant is *claiming less* than the full scope of his disclosure." The opinion, at page 195, goes on to state "But, as we said in In re Wertheim, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976): Inventions are constantly made which turn out not to be patentable, and applicants frequently discover during the course of prosecution that only a part of what they invented and originally claimed is patentable. It is for the inventor to decide what *bounds* of protection he will seek. In re Saunders, 58 CCPA 1316, 1327, 444 F.2d 599, 607, 170 USPQ 213, 220 (1971)." The opinion further states that "The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of §112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute. All that happened here is that appellants narrowed their claims to avoid having them read on a lost interference count." Finally, the opinion concludes "Here, as we hold on the facts of this case, the 'written description' in the 1963 specification supported the claims in the absence of the limitation, and that specification, having described the whole, necessarily described the part remaining. The facts of the prosecution are properly presented and relied on, under these circumstances, to indicate that appellants are merely excising the invention of another, to which they are not entitled, and are not creating an 'artificial subgenus' or claiming 'new matter.' "

The instant application. The facts of the instant case are analogous to those of In re Johnson discussed above. The Examiner acknowledges that the specification teaches polypeptides that comprise the fragments as recited in the claims. The Specification also teaches the specific

polypeptides recited in the instant claims. The specification provides ample basis for claims of the instant scope as the specification/disclosure is clearly directed to polypeptides of the type claimed, where many specific choices (e.g., species) are disclosed for the polymorphic polypeptide, where a broad *class* was identified that not only encompasses, as recognized by the Examiner, but also specifically includes the claimed polymorphic species, and that some of the many choices for the originally disclosed polypeptides are not instantly present in the protection sought, "because appellant is *claiming less* than the full scope of the disclosure."

As stated under MPEP 2173.05(i), a lack of literal basis in the specification for a negative limitation is not sufficient to establish a *prima facie* case for lack of descriptive support. Applicants contend that, as recognized and acknowledged by the Examiner, that the originally filed disclosure would have conveyed the claimed polypeptide species to one of ordinary skill in the art. ECDIIIa variant containing polypeptides, both comprising the ECDIIIa or sub fragments thereof are indeed encompassed within the original specification teachings. The independent claims have merely been amended to delineate the variant residues, including subfragment residues. Support for this amendment is explicitly found in Table 1 on page 33 of the originally-filed specification (see also, for example, original claim 27 reciting "ECDIIIa variant sequence"). Additionally, the specification recites that "[t]his result demonstrates that in the human population there are several variations in the intron-8 encoded domain that could lead to altered biochemical and biological properties among ECDIIIa-containing protein variants" (page 32, lines 21-23). Additionally, the specification at page 14, lines 6-8. recites "[f]or the production of antibodies, various host animals may be immunized by injection with *e.g.*, polyhistidine-tagged ECDIIIa variant polypeptides, truncated ECDIIIa variant polypeptides, functional equivalents of the ECDIIIa variants or mutants of the ECDIIIa region." Additionally, the specification teaches that "PCR, or reverse transcription can be utilized to identify nucleotide variation within the ECDIIIa domain" (page 17, lines 19-20).

Additionally, as stated in Dr. Gail Clinton's Declaration of record (see page 5, paragraph 5, of Declaration of Dr. Gail Clinton 19 April 2003, of record in this case), "[t]he discovery of these novel polymorphisms was precisely the reason that the present application was filed. The Herstatin sequence of the earlier U.S. patent application (09/234,208) was already disclosed and claimed in that application, and it was the primary purpose of the present application to claim additional polymorphisms, while not claiming the previously claimed Herstatin. In Example 11 of the present application, the 1999 Doherty et al. PNAS paper (which lists the previously claimed Herstatin) was cited in the introduction. Example 11 then goes on to describe the additional, different polymorphisms by their nucleotide and deduced amino acid sequence. These additional variations in the intron-8 encoded domain were discovered in the human population and Table 1 sets forth those variants, including originally identified variant 11. Said another way, while Table 1 of Example 11 lists the Doherty et al sequence as variant 11 along with the additional polymorphisms (variants 1-10), the purpose of the table is to set forth and summarize additional variants of the intron-8 encoded domain that had been discovered to the time of the filing of this patent application." The specification, therefore, discloses new polymorphic variants and ECDIIIa variant fragments of about 50 to about 79 amino acids. For example, the specification teaches ECDIIIa subfragments and teaches variants with the subfragment region. It would be an absurdity to construe the facts such that Applicants would not be entitled to claim a subfragment comprising any of the variant amino acids disclosed. Applicants are the first to describe such variants and this was precisely why the present application was filed, as declared by the Applicants.

Applicants respectfully contend that given the teachings of the specification, the Examiner's position is unsupported, is inconsistent with the facts, inconsistent with MPEP 2173.05(i), and contrary to relevant U.S. case law on this issue, including that of *In re Johnson*, 558 F.2d 1008,

1019, 194 USPQ 187, 196 (CCPA 1977), cited in MPEP 2173.05(i), and other references cited therein.

In conclusion, even if one implies a negative limitation or proviso clause as urged by the Examiner, there is no requirement under U.S. patent law to have a "literal basis" for such negative limitation or proviso clause. There is no requirement, contrary to the Examiner's urging, under U.S. Patent law that the specification provide "literal support" for a limitation that the fragments must comprise the residues that are different from the previously disclosed Herstatin. The specification not only teaches polypeptides that comprise the fragments as recited in the claims, but also teaches the specific polypeptides recited in the instant claims. Therefore, under *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977), and the MPEP 2173.05(i) the specification provides more than ample support for any such implied negative limitation or proviso. In any event, Applicants are in fact entitled to "carve out" a portion of the disclosed subject matter, whether it be done by merely claiming a portion of the invention, or through a negative limitation or proviso clause.

Applicants, therefore, respectfully request reconsideration and withdrawal of the Examiner's alleged new matter rejection.

Applicants respectfully contend that all claims are allowable as presented herein.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request entry of the present Amendment and allowance of all claims as provided herein above. The Examiner is encouraged to phone Applicants' attorney, Barry L. Davison, to resolve any outstanding issues and expedite allowance of this application.

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Enclosure: In re Johnson, 194 USPQ 187 (CCPA 1977)